REMARKS

INTRODUCTORY COMMENTS:

In a previous Office Action, the Examiner required restriction between six groups of claims, i.e., Groups I-VI, and applicants elected the claims of Group I, with traverse. The Examiner had also required election between the six species, i.e., species (1)-(6), and applicants elected species (1), without traverse. In the Office Action under reply, the Examiner made final the restriction requirement. As a result, the non-elected claims 59-80 were canceled and claims 1-58 are pending. Claims 11-18, 55 and 57 stand withdrawn from consideration as being directed to non-elected species, and only claims 1-10, 19-54 and 56 are addressed in this Office Action.

The drawings have been objected to as containing improper reference numerals or improper correspondence with the specification. Accordingly, the Examiner contends that the drawings fail to comply with 37 CFR §§1.84(p)(4) and 1.84(p)(5) and has required proposed drawing corrections, corrected drawings or amendment to the specification.

Claims 1-10, 19-54, and 56 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite. The pending claims also stand rejected over the art, as follows:

- (1) Claims 1-10, 19-33, 38-49, 54 and 56 are rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 5,874,214 to Nova et al.;
- (2) Claims 1, 43, and 56 stand rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,342,349 to Virtanen et al.; and
- (3) Claims 1 and 34-37 stand rejected under 35 U.S.C. §103(a) as obvious over Nova et al. in view of U.S. Patent No. 5,922,617 to Wang et al.

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The objections to the drawings and the claim rejections are addressed in part by the above amendments and are otherwise traversed for reasons that are discussed in detail below. For the Examiner's convenience, the pending claims upon entry of these amendments (claims 1, 3-58) are set forth in Appendix C.

THE ABOVE AMENDMENTS:

The specification has been amended to provide the serial number of a U.S. patent application referenced in the specification, to update the location of Picoliter Inc, and to correct a typographical error. In addition, the specification has been amended to identify item 25 in FIG. 2 as an integrated cartridge. These minor corrections in no way introduce new matter.

Claims 59-80 have been canceled as a result of restriction. Cancellation of these claims is without prejudice and without intent to abandon any originally claimed subject matter. In addition, claim 2 has been canceled to eliminate duplicative recitation of claim elements, in view of the amendment to independent claims 1, 50, 54, and 56.

Independent claims 1, 50, 54 and 56 have been amended to clarify the inventive subject matter and to expedite prosecution. Each of these claims sets forth a device comprising a substrate having an integrated indicator that exhibits a response to a condition, wherein the response is detectable *for at least one minute after removal from the condition*. This is supported in the specification, for example, on page 4, lines 11-13, and in claim 2 as filed. As claim 2 has been cancelled, claim 3 has been amended to depend from claim 1 instead of claim 2.

Thus, no matter has been introduced by way of any these amendments and entry thereof is proper and requested.

OBJECTION TO THE DRAWINGS

The Examiner objects to the drawings as failing to comply with 37 CFR §1.84(p)(4) because the reference numeral 13 has been used to refer a disk in FIG. 1, a well plate in FIG. 2, and a rectangular slide in FIG.3. Similarly, the Examiner also objected to the use of the reference numeral 15 to refer to an exterior surface in FIG. 1 and an interior surface in FIG. 2. In response, applicants point out that the disk, the well plate, and the rectangular slide each serves as the substrate of the device as disclosed and claimed. See, e.g., claims 43-46 and page 14, lines 7-9. As such, all items indicated by reference numeral 13 function as the substrate of the invention for each of the embodiments depicted in the figures. Similarly, all items indicated by reference numeral 15 function as the surface of the substrate to which the molecular probes are (or may be) attached. Accordingly, the drawings comply fully with 37 CFR §1.84(p)(4), and applicants respectfully traverse the Examiner's objection to the drawings on this basis.

The Examiner also objects to FIGS. 2 and 3 as failing to comply with 37 CFR §1.84(p)(5) as containing references numerals or letters that do not appear in the specification. With respect to FIG. 2, applicants hereby submit a proposed drawing correction, as indicated in Appendix D, and have amended the specification to correspond to the drawing correction. In addition, applicants point out that the reference letter E, referring to the dotted line in FIG. 3, is mentioned in the specification on page 6, lines 20-22. Accordingly, applicants respectfully request withdrawal of the objection to the drawings as failing to comply with 37 CFR §1.84(p)(5).

REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH:

Claims 1-10, 19-54, and 56 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite. The term "integrated indicator" is objected to because, according to the Examiner, "it is unclear how it relates to the probes." Similarly, the Examiner objects to the term "condition" as failing to point out whether the condition refers to "the interaction of the probes with the analytes of the probes...or the environmental 'condition' affecting the probes and analytes interactions." Applicants respectfully traverse the rejection.

With respect to the term "integrated indicator," applicants point out that it is specifically recited in the claims that probes are attached to a surface of a substrate and that the integrated indicator is a part of the substrate. In some instances, as depicted in FIG. 1 and discussed on page 14, line 20, to page 15, line 20, an integrated indicator may be located on the same surface as the probes. Alternatively, as depicted in FIG. 2 and discussed on page 17, lines 1-21, integrated indicators and the probes may be provided on a different surface of the same substrate. Furthermore, different types of environmental condition indicators are discussed on page 20, line 27, to page 26, line 7. Thus, the relationship between the probes and integrated indicator is unambiguously set forth in the application as filed.

Similarly, applicants disagree with the Examiner's statement that the term "condition" is unclear. It is explicitly set forth in the claims that the term "condition" refers to that to "which the substrate may be exposed." In addition, the specification is replete with examples of different types of conditions to which the substrate may be exposed. For instance, as discussed on page 13, line 11-17, the condition may correspond to the facilitation, enhancement, hindrance or prevention of target-probe interaction. In addition, as discussed on page 31, lines 10-15, the

condition may relate to an experimental procedure and assay performance. Notably, the term "hybridization conditions" is expressly defined on page 10, line 22, to page 11, line 2. One of ordinary skill in the art would therefore understand other references to the term "condition" have an analogous meaning.

Accordingly, applicants respectfully request reconsideration and withdrawal of this rejection.

<u>THE 35 U.S.C. §102(B) REJECTION OF CLAIM 1-10, 19-33, 38-49, 54, AND 56 AS ANTICIPATED BY NOVA ET AL.</u>:

Claims 1-10, 19-33, 38-49, 54 and 56 stand rejected as anticipated by Nova et al. According to the Examiner, Nova et al. discloses a device that is a combination of matrix materials with programmable date storage or recording devices. Citing column 37, lines 31-33, the Examiner states that the recording device can detect the occurrence of a reaction and records the event in memory. In addition, the Examiner cites column 38, lines 49-63, column 49, lines 53-63, and column 53, lines 44-50, as disclosing that the recording device may include "a temperature sensor to record the temperature of the reaction." Characterizing the remaining features recited in the claims as "variations in parameters which are routinely modified in the art," the Examiner states that other sections of Nova et al. either specifically describe the features or render the features obvious.

It is axiomatic that for a reference to anticipate a claim, a cited reference must disclose each and every element of the claim. *In re Spada*, 15 USPQ2d 1655 (Fed. Cir. 1990). Unless there is "identity of invention," such that all claim elements are disclosed in a single reference, there can be no anticipation under 35 U.S.C. §102. Here, all pending independent claims as amended, i.e., claims 1, 50, 54 and 56, are directed to devices each having at least one integrated indicator that exhibits a response when exposed to a condition, wherein the indicator response is *detectable after removing the indicator from the condition*. This feature is clearly absent from Nova et al. Although Nova et al. describes the use of a temperature sensor, there is no disclosure relating to whether the response of the temperature sensor to a particular temperature is detectable after the temperature sensor is removed from the particular temperature environment. Instead, one of ordinary skill in the art would read Nova et al. as describing a temperature sensor for "real-time" temperature monitoring. Such "real-time" temperature monitoring does not

involve an indicator response to a condition that is detectable after the indictor is removed from the condition. In order to expedite prosecution and further distinguish the claimed subject matter over Nova et al., however, applicants have amended the claims to recite that the indicator response is detectable for *at least one minute* after removal from the condition. This feature, too, is absent from Nova et al. Accordingly, Nova et al. does not anticipate any claims.

In addition, this feature renders all claims nonobvious over Nova et al. As pointed out by the Examiner, Nova et al. describes a combination of a matrix with a memory in which a temperature-sensing device may be provide that is electrically connected to the recording device for recording the temperature detected by the sensing device. As further discussed in Nova et al. in column 8, lines 48-52, an electrical signal may be generated as a result which allows the recording device to be written to in less than five seconds, most preferably in about 1 millisecond or less. Thus, Nova et al. merely describes a combination of a matrix with a recording device in which the temperature-sensing device, upon exposure to a particular temperature, responds by instantaneously generating a transient electrical signal. The transient electrical signal, in turn, may be written to the recording device. While the recording device may serve to provide a record of the particular temperature experience by the temperature-sensing device, the response of the temperature of the temperature-sensing device, i.e., transient electrical signal itself, would not be detectable for at least one minute after the temperature-sensing device is removed from the particular temperature. Thus, Nova et al. does not suggest a device comprised of a substrate having an integrated indicator that exhibits a response that is detectable for at least one minute after removal of the indicator from the condition triggering the response.

In addition, Nova et al. effectively teaches away from the invention as claimed. As discussed above, Nova et al. describes a combination of a matrix with a recording device, wherein the recording device may record the particular temperature to which the temperature-sensing device has been exposed. With such a record, one skilled in the art would not think that there would be any need for the response of the temperature-sensing device itself to remain detectable. In particular, one skilled in the art, upon reading Nova et al., would not recognize a need for the electrical signal to be generated and detectable for over one minute. Given that Nova et al. teaches a programmable recording device that appears to a be a critical element of the described combination and that a shorter programming time is preferred over a longer

programming time, Nova et al. effectively teaches away from an indicator whose response to a condition is detectable for at least one minute after removal from the condition.

Thus, applicants respectfully request reconsideration and withdrawal of this rejection.

THE 35 U.S.C. §102(E) REJECTION OF CLAIMS 1,43, AND 56 AS ANTICIPATED BY VIRTANEN ET AL.:

Claims 1, 43 and 56 stand rejected as anticipated by Virtanen et al. In issuing this rejection, the Examiner states that Virtanen et al. discloses a device comprising an optical disk having analyte specific signal elements that are cleaveable and that a signal is detected from the cleave signal element. According to the Examiner, "[t]he cleaveable signal element comprises a signal responsive moiety (indicator) attached to the cleaveable spacer at its signal responsive end (probe)." In addition, the Examiner contends that the cleaveable spacer has a substrate-attaching end.

Applicants traverse this rejection and submit that the Examiner has mischaracterized the role of the cleavable signal elements described in Virtanen et al. The cleavable signal elements are merely probes selected to interact with a corresponding target (e.g., a probe nucleic acid sequence that may hybridize with a complementary target nucleic acid sequence in a sample, as described in column 6, lines 58-64). The signal responsive moiety simply indicates whether binding has occurred. See column 5, lines 58-60. In essence, Virtanen et al. describes an optical disk having probes attached to a surface thereof, wherein the probes are cleaved when they bind with a target. In other words, Virtanen et al. merely describes an optical disk with probes that generate a signal when they interact with a corresponding target. Accordingly, a signal generated by a probe/target interaction differs from the response of a condition indicator in that the signal generated by the probe/target interaction generally provides a *specific* assay result, e.g., whether a target is present in a sample. In contrast, the indicator response, triggered by exposure to a condition to which the substrate may be exposed, is generally more global in nature and may be applicable to all probe/target interactions. For example, the indicator response may indicate whether all probes have been exposed to a particular temperature, thereby indicating whether the assay was carried out within an appropriate temperature range. Virtanen et al. simply does not contain any disclosure relating to an integrated indicator.

Applicants therefore point out that the pending claims are directed to devices comprising a substrate having **both** molecular probes and an integrated indicator as well as precursors to such devices. Since Virtanen et al. does not disclose a device that has an integrated indicator that exhibits a response that is detectable for at least one minute after removing the indicator from a response-triggering condition, Virtanen et al. does not anticipate the pending claims.

Accordingly, applicants respectfully request reconsideration and withdrawal of this rejection as well.

THE 35 U.S.C. §103(A) REJECTION OF CLAIMS 1 AND 34-37 AS OBVIOUS OVER NOVA ET AL. IN VIEW OF WANG ET AL.:

Claims 1 and 34-37 stand rejected as obvious over Nova et al. in view of Wang et al. While the Examiner states that Nova et al. does not disclose an array comprising 10, 50,000, 200,000, or 1,000,000 probes on a substrate, the Examiner states that Wang et al. discloses a microarray containing 10 or more probes. In addition, the Examiner has characterized Wang et al. as suggesting that the number of individual addressable sites on an array would depend on the nature of the bound component, the source of a signal, the nature of the signal being detected, the nature of the bound array, or the manner in which the array is produced. As a result, the Examiner states that Nova et al. and Wang et al. are combinable and teach a device for detecting multiple analytes.

Applicants traverse this rejection because the cited patents, when combined, do not teach or suggest all the claim limitations. As discussed above, Nova et al. does not suggest a device comprised of a substrate having an integrated indicator that exhibits a response that is detectable for at least one minute after removal of the indicator from the condition triggering the response. In addition, the signal to which the Examiner refers in Wang et al. relates to that which is generated by probes, not by an integrated indicator. Thus, the technology discussed in Wang et al. is generally similar to that described by Virtanen et al. in that the technology provides probes that generate a signal when they interact with a corresponding target. Like Virtanen et al. and Nova et al., Wang et al. also fails to teach or suggest an integrated indicator that exhibits a response that is detectable for at least one minute after removal of the indicator from the condition triggering the response. Accordingly, withdrawal of this rejection is warranted.

CONCLUSION

For all of the above reasons, it is submitted that this application comports with all requirements of 35 U.S.C. §112, second paragraph and that the pending claims define an invention that is patentable over the art. As the application should now be in condition for allowance, a prompt indication to that effect would be appreciated.

If the Examiner has any questions concerning this communication, he is welcome to contact the undersigned attorney at (650) 330-0900.

Respectfully submitted,

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APPENDIX A

REDACTIONS INDICATING AMENDMENTS MADE TO THE SPECIFICATION (UNDERLINING INDICATING ADDITIONS, STRIKETHROUGHS INDICATING DELETIONS)

Please amend the paragraph on page 3, line 13-25 as follows:

Please amend the paragraph on page 14, line 7-19 as follows:

The substrate of the device may take a number of forms. For example, the substrate may comprise a disk, tape, well plate, a slide, or other objects commonly used as a substrate. Optionally, the substrate may further contain machine-readable information and/or a medium on which information may be written. Such medium is typically selected to contain electronic information and may be noncoplanar with respect to the surface on which the molecular probes are attached. Optimally, the medium is writable from a surface that opposes the surface on which the molecular probes are attached. Devices comprising a substrate having molecular moieties attached to a surface thereof and containing machine-readable information are described

in U.S. Patent Application Serial No. ______09/712,818, ("Integrated Device with Surface-Attached Molecular Moieties and Related Machine-Readable Information"), inventors Ellson, Foote and Mutz, filed on November 13, 2000 and assigned to Picoliter, Inc. (Cupertino Sunnyvale, California).

Amend the paragraph on page 17, line 22, to page 18, line 18, as follows:

Optionally, the well plate 13 is attached to a cartridge base 29 to form an integrated cartridge 25 and to define a cartridge interior 31. A magnetic disk 33 is generally interposed between well plate 13 and the cartridge base 29 within the cartridge interior 31. The disk 33 is a generally flat and circular piece having an upper surface 35 and a lower surface 37. A cylindrical hub 39 extends perpendicularly from the center of the lower surface 37 of the disk 33 through circular opening 41 of the cartridge base 29. The disk is free to rotate about its hub in a generally free-floating manner. The lower surface 37 is coated with magnetic storage medium 43 that allows a spiral track 23 to be formed therein to magnetically store machine-readable information related to the molecular probes. Also optionally located in the cartridge base 29 is a rectangular opening 45 that provides external access to the magnetic disk contained in the cartridge interior 31. A slidable spring-loaded panel 47 covers the opening 45 in order to protect the magnetic medium on the disk from damage when the disk is not in use. As shown, the slidable panel 47 is positioned such that it does not cover the opening, thereby providing a magnetic reader access to the magnetic medium on the disk. Thus, the information contained in the spiral track 23 is ready for reading by a magnetic reader. Design, construction and use of such magnetic readers are well known in the art. For example, the magnetic reader may engage the disk by gripping the portion of the hub 39 that is accessible to the exterior to the cartridge and spinning the disk. This allows information contained in the spiral track to be read. As the information relating to the attached probes is located within the disk as a spiral track 23 rather than on the interior surfaces 15 of the well plate to which the molecular probes 21 are attached, it is evident that the information is located in a discrete region of the disk that is noncoplanar with respect to the surfaces 15. Optionally, one or more of the interior surfaces 15 may be covered with a protective layer (not shown) that protects the probes from damage as a result of improper

handling. Devices for sealing well plates are commercially available from many sources including TekCel Corporation (Hopkinton, MA). Such protective coatings may also be adapted to protect the integrated indicators.

Amend the paragraph on page 20, lines 1-12, as follows

Optionally, information relating to the molecular probes is contained in an electronic microchip 23 that provides sufficient memory to store such information. As shown, the microchip 23 is embedded in the slide 13. Such a microchip 23 may be partially exposed at surface 17, as shown in FIG. 3, or located entirely within the substrate. Such microchips are often employed in smart cards, e.g., plastic cards resembling a credit card that contains a computer chip, which enables the holder to perform various operations, such as mathematical calculations, paying of bills, and the purchasing of goods and services. Use of smart card technology in conjunction with nucleotidic probes is described in U.S. Patent Application Serial No. _____09/712,818 ("Integrated Device with Surface-Attached Molecular Moieties and Related Machine-Readable Information"), inventors Ellson, Foote and Mutz, filed on November 13, 2000 and assigned to Picoliter, Inc. (Cupertine Sunnyvale, California).

Amend the paragraph on page 30, line 18, to page 31 line 6, as follows.

Alternatively, an oligomer may be synthesized prior to attachment to the substrate surface and then "spotted" onto a particular locus on the surface using the methodology of the invention as described in detail above. Again, the oligomer may be an oligonucleotide, an oligopeptide, or any other biomolecular (or nonbiomolecular) oligomer moiety. Preparation of substrate-bound peptidic molecules, e.g., in the formation of peptide arrays and protein arrays, is described in copending patent application U.S. Serial No. 09/669,997 ("Focused Acoustic Energy in the Preparation of Peptidic Arrays"), inventors Mutz and Ellson, filed on September 25, 2000 and assigned to Picoliter, Inc. (Cupertino Sunnyvale, California). Preparation of substrate-bound oligonucleotides, particularly arrays of oligonucleotides wherein at least one of the oligonucleotides contains partially nonhybridizing segments, is described in co-pending patent

APPENDIX B

REDACTED CLAIMS INDICATING AMENDMENTS MADE (UNDERLINING INDICATING ADDITIONS, STRIKETHROUGHS INDICATING DELETIONS)

1. (Amended) A device comprising a substrate having a plurality of different molecular probes attached to a surface thereof and an integrated indicator that exhibits a response when exposed to a condition to which the substrate may be exposed,

wherein each different molecular probe is selected to interact with a corresponding target, and further wherein the indicator response is detectable <u>for at least one minute</u> after removing the indicator from the condition.

- 3. (Amended) The device of claim 21, wherein the indicator response to the condition is detectable for at least 1 hour after removing the substrate from the condition.
- 50. (Amended) A device comprising a substrate having a plurality of molecular probes attached to a surface thereof and a plurality of different integrated indicators, each indicator selected to exhibit a response when exposed to one of a plurality of conditions to which the substrate may be exposed, wherein the molecular probes are selected to interact with corresponding targets, and further wherein the response is detectable <u>for at least one minute</u> after removing the indicator from the condition
- 54. (Amended) A device comprising a substrate having a plurality of nucleotidic molecular probes attached to a surface thereof and an integrated indicator that exhibits a response when exposed to a condition to which the substrate may be exposed, wherein the nucleotidic molecular probes are selected to interact with corresponding targets, and further wherein the response is detectable <u>for at least one minute</u> after removing the indicator from the condition.
- 56. (Amended) A device comprising a substrate having a surface adapted for attachment to a plurality of molecular moieties and an integrated indicator that exhibits a response when

exposed to a condition, wherein the response is detectable <u>for at least one minute</u> after removing the indicator from the condition.

APPENDIX C

PENDING CLAIMS UPON ENTRY OF THE AMENDMENT

1. (Amended) A device comprising a substrate having a plurality of different molecular probes attached to a surface thereof and an integrated indicator that exhibits a response when exposed to a condition to which the substrate may be exposed,

wherein each different molecular probe is selected to interact with a corresponding target, and further wherein the indicator response is detectable for at least one minute after removing the indicator from the condition.

- 3. The device of claim 1, wherein the indicator response to the condition is detectable for at least 1 hour after removing the substrate from the condition.
- 4. The device of claim 3, wherein the indicator response to the condition is substantially permanently detectable.
- 5. The device of claim 1, wherein the condition is an environmental condition that allows for target-probe interaction.
- 6. The device of claim 5, wherein the environmental condition is a predetermined temperature.
- 7. The device of claim 6, wherein the predetermined temperature is a maximum temperature.
- 8. The device of claim 7, wherein the maximum temperature is about 60°C to about 90°C.
- 9. The device of claim 6, wherein the predetermined temperature is a minimum temperature.

- 10. The device of claim 9, wherein the minimum temperature is about 35°C to about 45°C.
- 11. The device of claim 5, wherein the environmental condition is a predetermined water content.
- 12. The device of claim 5, wherein the environmental condition is a chemical concentration.
- 13. The device of claim 12, wherein the chemical concentration is a formamide concentration,
- 14. The device of claim 12, wherein the chemical concentration comprises a pH of about 5 to about 9.
- 15. The device of claim 12, wherein the chemical concentration is a salinity of about 0.01 molar to about 8 molar.
- 16. The device of claim 1, wherein the condition is the presence of a chemical moiety that affects the target-probe interaction.
- 17. The device of claim 16, wherein the chemical moiety hinders the target-probe interaction.
- 18. The device of claim 16, wherein the chemical moiety enhances the target-probe interaction.
 - 19. The device of claim 1, wherein the indicator response is optically detectable.
 - 20. The device of claim 19, wherein the indicator response is fluorescently detectable.

- 21. The device of claim 1, wherein the indicator response is magnetically detectable.
- 22. The device of claim 1, wherein the indicator response is electrically detectable.
- 23. The device of claim 1, wherein the indicator response is machine detectable.
- 24. The device of claim 1, wherein the response occurs after exposure of the indicator to the condition for at least a predetermined period.
- 25. The device of claim 24, wherein the predetermined period is about 1 minute to about 28 hours.
- 26. The device of claim 25, wherein the predetermined period is about 5 to about 10 hours.
- 27. The device of claim 26, wherein the predetermined period is about 6 to about 8 hours.
 - 28. The device of claim 1, wherein the molecular probes are biomolecular.
 - 29. The device of claim 28, wherein the molecular probes are nucleotidic.
 - 30. The device of claim 28, wherein the molecular probes are peptidic.
 - 31. The device of claim 28, wherein the molecular probes are oligomeric.
 - 32. The device of claim 28, wherein the molecular probes are polymeric.

- 33. The device of claim 1, wherein the molecular probes are arranged in an array on the substrate surface.
- 34. The device of claim 33, wherein the array comprises at least about 10 probes per square centimeter of substrate surface.
- 35. The device of claim 34, wherein the array comprises at least about 50,000 probes per square centimeter of substrate surface.
- 36. The device of claim 35, wherein the array comprises at least about 200,000 probes per square centimeter of substrate surface.
- 37. The device of claim 36, wherein the array comprises at least about 1,000,000 probes per square centimeters of substrate surface.
- 38. The device of claim 1, wherein the substrate further contains machine-readable information.
- 39. The device of claim 38, wherein the substrate further comprises a medium on which information may be written.
- 40. The device of claim 39, wherein the medium is selected to contain electronic information.
- 41. The device of claim 39 wherein the medium is noncoplanar with respect to the surface on which the molecular probes are attached.
- 42. The device of claim 41, wherein the medium is writable from a surface that opposes the surface on which the molecular probes are attached.

- 43. The device of claim 1, wherein the substrate comprises a disk.
- 44. The device of claim 1, wherein the substrate comprises a tape.
- 45. The device of claim 1, wherein the substrate comprises a well plate.
- 46. The device of claim 1, wherein the substrate comprises a slide.
- 47. The device of claim 1, wherein the targets represent portions of a single molecule.
- 48. The device of claim 1, wherein the targets represent portions of single cell.
- 49 The device of claim 1, wherein the integrated indicator comprises nucleotidic material.
- 50. (Amended) A device comprising a substrate having a plurality of molecular probes attached to a surface thereof and a plurality of different integrated indicators, each indicator selected to exhibit a response when exposed to one of a plurality of conditions to which the substrate may be exposed, wherein the molecular probes are selected to interact with corresponding targets, and further wherein the response is detectable for at least one minute after removing the indicator from the condition.
- 51. The device of claim 50, wherein the molecular probes are selected to interact with corresponding targets when exposed to at least one of the plurality of conditions.
- 52. The device of claim 51, wherein the molecular probes are selected to interact with corresponding targets when exposed to all of the conditions.
- 53. The device of claim 52, wherein the molecular probes are selected to interact with corresponding targets when exposed to all of the conditions simultaneously.

- 54. (Amended) A device comprising a substrate having a plurality of nucleotidic molecular probes attached to a surface thereof and an integrated indicator that exhibits a response when exposed to a condition to which the substrate may be exposed, wherein the nucleotidic molecular probes are selected to interact with corresponding targets, and further wherein the response is detectable for at least one minute after removing the indicator from the condition.
- 55. The device of claim 54, wherein the condition represents a hybridization condition between the probes and targets.
- 56. (Amended) A device comprising a substrate having a surface adapted for attachment to a plurality of molecular moieties and an integrated indicator that exhibits a response when exposed to a condition, wherein the response is detectable for at least one minute after removing the indicator from the condition.
- 57. The device of claim 56, wherein the condition is suitable for attaching the plurality of molecular moieties to the substrate surface.
- 58. The device of claim 56, wherein the condition is not suitable for attaching the plurality of molecular moieties to the substrate surface.